Surgical Model of Menopause Symptoms: GABA'S Role in Anxiety and Hot Flashes

Anna Frink[1]

[1]Department of Anatomy and Cell Biology, Indiana University School of Medicine, Indianapolis, IN, 46202

Menopause is the permanent cessation of the primary functions of the human ovaries: the ripening and release of the ova, and the release of hormones that create the uterine lining. The transition from a reproductive to non-reproductive state is a result of a reduction in sex hormone production by the ovarian follicular cells due to their degeneration. For some women, the accompanying signs of and effects that can occur during the menopause transition years can significantly disrupt their daily activities and sense of well-being; symptoms include vasomotor instability (hot flashes and night sweats), anxiety, and sleep disruption. Unfortunately, animal modeling to understand these symptoms, particularly "hot flashes" has been limited and lacks predictive and construct validity. We have developed a novel model of "hot flashes" by injecting a 3 mg/kg (intraperitoneal administration) dose of the anxiogenic drug FG-7142 (a partial inverse agonist at the benzodiazepine site on the $GABA_A$ receptor) following bilateral ovariectomy. Previous work in our lab has determined that this injection elicits a rapid, 9° Celsius increase in tail skin temperature (the indicator of the "hot flash" response in a rat) in ovariectomized rats but not in sham-operated control rats. However, the neural sites that mediate this response are unknown. We hypothesized that there are significant differences in either the anatomical sites involved in the "hot flash" response in ovariectomized rats or the extent of activation of the same neural sites. To test this hypothesis, female rats were either bilaterally ovariectomized or sham-ovariectomized; following recovery, rats were given a 3 mg/kg dose of FG-7142 or vehicle and perfused 90 min later. Tissue was processed and stained for the immediate early gene product *c-fos*. It was determined that the ovariectomized rats had a hyperactive response in the hypothalamic brain region associated with anxiety and thermoregulation (i.e., dorsal medial hypothalamus).

Mentors: Philip L. Johnson, Department of Anatomy and Cell Biology, Indiana University School of Medicine; Lauren M. Federici, Department of Anatomy and Cell Biology, Indiana University School of Medicine